

REMARKS

Claims 1-70 are pending. Claims 1-11 and 13-64 are withdrawn from consideration, and claims 65-70 are canceled. Claim 12 is amended, and new claims 71-76 are added.

Support for the Amendments

Support for the amendments can be found in the specification and claims as originally filed. For example, support for the amendment of claim 12, which recites "3 months" is found at page 69, lines 11-23; support for the amendment of claim 12, which recites "suppresses proliferation" is found at page 1, lines 8-10; support for new claims 71, 72, 75, and 76, which recite "human cancer cells" or "human prostate cancer cells" is found, for example, at page 1, lines 6-10; support for new claims 73 and 74 is found, for example, at page 69, lines 11-23, at page 12, lines 25-34, and at page 79, lines 19-25. No new matter has been added.

The amendments to the claims should in no way be construed as acquiescence to any of the Examiner's rejections and were made solely to expedite the prosecution of the application. Applicant reserves the right to pursue the claims as originally filed in this or a separate application(s).

Traversal of Restriction Requirement

The Examiner acknowledges that Applicants' claims recite a technical feature that distinguishes the claimed invention over Veldscholte et al., (Biochem. Biophys. Res. Comm. 173:534-540, 1990), Culig et al., (Br. J. Cancer 81:242-251, 1999), and Furr et al., (Urology 47:13-32, 1996), each of which was cited in the Office action mailed January 12, 2007. However, the Examiner maintains the restriction requirement based on the allegation that Applicants' claims lack a special technical feature over Hara et al. (Cancer Res. 63:149-153, 2003).

Hara is not available as prior art in view of Applicants' submission on February 12, 2004 in the present application of a certified copy of priority application JP 2002-255612, filed August 30, 2002, and by the submission herewith of a certified English language translation of the priority application, thereby perfecting Applicants' claim to priority. Applicants respectfully request reconsideration of the Restriction Requirement with respect to

this reference, and rejoinder of at least groups I (claims 1-4), II (claims 5-8 and 18) and V (claim 12).

Objection to the Specification

The Examiner objects to the specification as allegedly lacking a cross-reference to priority documents and for allegedly failing to properly identify the trademarks polysorbate 80 and Triton X-100. These objections are overcome by the present amendment of the specification.

Rejections under 35 U.S.C. §112, Second Paragraph

The Examiner rejects claim 12 under 35 U.S.C. §112, second paragraph, as allegedly indefinite. Applicants respectfully disagree and traverse the rejection.

However, without acquiescing in any way to the rejection and in order to expedite prosecution of the application, the present amendment obviates the rejection of claim 12 under 35 U.S.C. §112, second paragraph. Accordingly, Applicants request that this rejection be withdrawn.

Rejections Under 35 U.S.C. §102

The Examiner rejects claim 12, which is directed to methods under 35 U.S.C. § 102(a) as allegedly anticipated by Hara *et al.* Cancer Res. 63:149-153, 2003; hereinafter “Hara”). This rejection is overcome by the submission on February 12, 2004 in the present application of a certified copy of priority application JP 2002-255612, filed August 30, 2002, and by the submission herewith of a certified English language translation of the priority application, thereby perfecting Applicants’ claim to priority under 35 U.S.C. 119(a)-(d) within the time period set in 37 CFR 1.55(a)(1). Applicants respectfully submit that the priority document satisfies the enablement and description requirements of 35 U.S.C. 112, first paragraph, and therefore antedates the Hara *et al.* reference. Thus, the rejection of claim 12 under 35 U.S.C. § 102(a) over Hara should be withdrawn.

The Examiner rejects claim 12 under 35 U.S.C. §102(b) as allegedly anticipated by Long *et al.* (*Cancer Research* 60: 6630-40, 2000; hereinafter “Long”) and by Foury *et al.* (*J.*

Steroid Biochem. Molec. Biol. 66: 235-40, 1998). Applicants respectfully disagree with the rejection and request that it be withdrawn.

For a reference to serve as the basis for an anticipation rejection that reference must disclose each and every element of present in the claim. M.P.E.P. 2131 “A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” *Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 2001). Long and Foury fail to disclose each and every aspect of Applicants’ invention as presently claimed, and therefore cannot destroy the novelty of the invention.

Claim 12 recites culturing cells of an androgen-sensitive-cancer in the presence of a test substance for at least three months. Neither Long nor Foury describe culturing the cells in the presence of a test compound for this length of time. Specifically, Long merely describes culturing the cells for nine days following treatment with a test compound (page 6631, right column, 2nd full paragraph under the heading “Cell Culture”). Similarly, Foury describes culturing cancer cells in the presence of a test compound for seven days (page 236, right column, 2nd full paragraph under the heading “Cell proliferation”). In sum, neither Long nor Foury describes culturing cancer cells in the presence of a test compound for at least 3 months; thus, neither Long nor Foury anticipates claim 12. Applicants respectfully request withdrawal of the rejection of claim 12 under 35 U.S.C. §102(b).

Rejections of Claim 12 Under 35 U.S.C. §103

Claim 12 is rejected under 35 U.S.C. §103(a) as being unpatentable over Taplin *et al.* (*Cancer Research* 59: 2511-2515, 1999; hereinafter “Taplin”) in view of Joly-Pharaboz *et al.* (*J. Steroid Biochem. Molec. Biol.* 55:67-76, 1995; hereinafter “Joly-Pharaboz”). For the reasons discussed below, Applicants respectfully disagree with the rejection, and request that it be withdrawn.

The test of obviousness requires that one compare the claimed “subject matter as a whole” with the prior art “to which said subject matter pertains” 35 U.S.C. § 103(a). To establish a *prima facie* case of obviousness, three criteria must be met. First, a suggestion or motivation to modify the reference or combine reference teachings must be present in the references or in the general knowledge present in the art. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim

limitations. M.P.E.P. 2143. The burden is on the Examiner to show that the references expressly or impliedly suggest all of the claim limitations. M.P.E.P. 2142. "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons skilled in the art." *In re Rouffet*, 149 F.3d 1350, 1357. In the absence of some teaching or suggestion to combine, no *prima facie* case of obviousness can be established, and the rejection is improper and must be withdrawn. *In re Fine*, 837 F.2d 1071, 1074.

Taplin describes hydroxyflutamide-activated androgen receptors having mutations at codon 874 (page 2514, right column, 1st full paragraph). As acknowledged by the Examiner, Taplin fails to describe *in vitro* methods of drug screening. In particular, as noted by the Examiner (Office Action mailed May 15, 2007, page 7, 4th paragraph), Taplin merely recognized that conventional therapies were not effective. Although Taplin states that "alternative methods to further block the AR-mediated signaling" (p. 2514, right column, last paragraph) are required, Taplin fails to teach or suggest how compounds having the desired properties are to be obtained, as Applicants do. Specifically, Taplin fails to teach or suggest methods for identifying compounds that do not induce antiandrogen drug resistance.

Joly-Pharaboz fails to remedy the deficiencies of Taplin. Joly-Pharaboz merely describes the effects of androgens on the proliferation of prostate cancer cell lines, and describes the culture of prostate cancer cell lines in the presence of a test compound for seven days (page 67, Abstract, and Figure 1). Joly-Pharaboz failed to recognize, as Applicants did, that culturing cells of an androgen-sensitive cancer in the presence of a test substance for at least three months; and identifying a test substance that suppresses proliferation of the cancer cells, could be used to identify an antiandrogen drug that does not induce antiandrogen drug-resistance.

In sum, neither Taplin nor Joly-Pharaboz teaches or suggests all of the limitations of the presently claimed invention. In particular, neither Taplin nor Joly-Pharaboz teaches or suggests culturing cells of an androgen-sensitive cancer in the presence of a test substance for at least three months; and identifying a test substance that suppresses proliferation of said cancer cells, thereby identifying an antiandrogen drug that does not induce antiandrogen drug-resistance. In the absence of such a teaching or suggestion, the skilled artisan would lack any motivation to modify the culture method described by Joly-Pharaboz to arrive at Applicants' long term screening method. Furthermore, in the absence of any teaching or

suggestion by the cited references, the skilled artisan would lack the requisite expectation of success to make such a modification.

New Claims 73-76

Applicants note that new claims 73-76 are readily distinguishable over the prior art. In particular, none of the cited references describes a cancer cell comprising a leucine or cysteine substitution for tryptophan at amino acid number 746 of SEQ ID NO:2 as recited in claim 73. Furthermore, none of the cited references describes a cell that further comprises an alanine substitution for threonine at amino acid number 882 of SEQ ID NO:2 as recited in claim 74. Accordingly, Applicants submit that independent claim 73, and claims 74-76, which depend from claim 73, are in condition for allowance, and such action is respectfully requested.

SUMMARY

In view of the above amendment, applicant believes the pending application is in condition for allowance.

Applicants believe that no fee is due to consider the present amendment. Nevertheless, the Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105.

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Respectfully submitted,

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